

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

Claims 1-530 (Canceled).

531. (Currently amended) A method of treating an angiogenic disease or condition in an animal comprising administering to the animal an effective amount of a metal-binding peptide which does not have a metal ion bound to it, having the formula; the sequence of the peptide being:

$$P_1 - P_2,$$

wherein:

$P_1$  is:

Xaa<sub>1</sub> Xaa<sub>2</sub> His[:] or

Xaa<sub>1</sub> Xaa<sub>2</sub> His Xaa<sub>3</sub>[:],

the  $P_1$  portion of the peptide being linear;

$P_2$  is (Xaa<sub>4</sub>)<sub>n</sub>;

Xaa<sub>1</sub> is the N-terminal amino acid of the peptide, Xaa<sub>1</sub> has an unsubstituted  $\alpha$ -amino group, and Xaa<sub>1</sub> is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

Xaa<sub>2</sub> is glycine, alanine,  $\beta$ -alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, asparagine, glutamic acid, glutamine, lysine, hydroxylysine, histidine, arginine, ornithine, phenylalanine, tyrosine, tryptophan, cysteine, methionine, or  $\alpha$ -hydroxymethylserine;

Xaa<sub>3</sub> is glycine, alanine, valine, lysine, arginine, ornithine, aspartic acid, glutamic acid, asparagine, glutamine or tryptophan;

Xaa<sub>4</sub> is any amino acid; and

n is 0-100;

or a physiologically-acceptable salt thereof.

532. (New) The method of Claim 531 wherein:

Xaa<sub>1</sub> is glycine, alanine, valine, leucine, isoleucine, serine, threonine, aspartic acid, glutamic acid, lysine, hydroxylysine, histidine, arginine, or  $\alpha$ -hydroxymethylserine, and

Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, glutamine, cysteine, methionine, lysine, hydroxylysine, histidine, arginine, or  $\alpha$ -hydroxymethylserine.

533. (Previously presented) The method of Claim 531 wherein Xaa<sub>1</sub> is aspartic acid, glutamic acid, arginine, threonine or  $\alpha$ -hydroxymethylserine.

534. (Previously presented) The method of Claim 531 wherein Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine.

535. (Previously presented) The method of Claim 531 wherein Xaa<sub>3</sub> is lysine.

536. (Previously presented) The method of Claim 531 wherein:

Xaa<sub>1</sub> is aspartic acid, glutamic acid, arginine, lysine, threonine, serine or  $\alpha$ -hydroxymethylserine,

Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine, asparagine, methionine, histidine or  $\alpha$ -hydroxymethylserine, and

Xaa<sub>3</sub>, when present, is lysine.

537. (Previously presented) The method of Claim 536 wherein Xaa<sub>1</sub> is aspartic acid or glutamic acid and Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine or  $\alpha$ -hydroxymethylserine.

538. (Previously presented) The method of Claim 537 wherein Xaa<sub>2</sub> is glycine, alanine, valine, leucine or isoleucine.

539. (Previously presented) The method of Claim 538 wherein P<sub>1</sub> is Asp Ala His or Asp Ala His Lys.

540. (Previously presented) The method of Claim 539 wherein P<sub>1</sub> is Asp Ala His Lys.

541. (Previously presented) The method of Claim 536 wherein Xaa<sub>1</sub> is arginine, lysine, threonine, serine or  $\alpha$ -hydroxymethylserine, and Xaa<sub>2</sub> is glycine, alanine, valine, leucine, isoleucine, threonine, serine or  $\alpha$ -hydroxymethylserine.

542. (Previously presented) The method of Claim 541 wherein P<sub>1</sub> is Thr Leu His, HMS HMS His or Arg Thr His.

543. (Previously presented) The method of Claim 531 wherein n is 0-10.

544. (Previously presented) The method of Claim 543 wherein n is 0-5.

545. (Previously presented) The method of Claim 544 wherein n is 0.

546. (Previously presented) The method of Claim 531 wherein P<sub>2</sub> comprises a metal-binding sequence.

547. (Previously presented) The method of Claim 546 wherein P<sub>2</sub> comprises one of the following sequences:

(Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>3</sub> His Xaa<sub>2</sub> Xaa<sub>5</sub>,  
(Xaa<sub>4</sub>)<sub>m</sub> His Xaa<sub>2</sub> Xaa<sub>5</sub>,  
(Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>5</sub> Xaa<sub>2</sub> His Xaa<sub>3</sub>, or  
(Xaa<sub>4</sub>)<sub>m</sub> Xaa<sub>5</sub> Xaa<sub>2</sub> His,

wherein Xaa<sub>5</sub> is an amino acid having a free side-chain -NH<sub>2</sub> and m is 0-5.

548. (Previously presented) The method of Claim 547 wherein Xaa<sub>5</sub> is Orn or Lys.

549. (Previously presented) The method of Claim 546 wherein P<sub>2</sub> comprises one of the following sequences:

[(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>5</sub>Xaa<sub>2</sub>HisXaa<sub>3</sub>]<sub>r</sub>,  
[(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>5</sub>Xaa<sub>2</sub>His]<sub>r</sub>,  
[(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>5</sub>Xaa<sub>2</sub>HisXaa<sub>3</sub>(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>5</sub>Xaa<sub>2</sub>His]<sub>r</sub>, or  
[(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>5</sub>Xaa<sub>2</sub>His(Xaa<sub>4</sub>)<sub>m</sub>Xaa<sub>5</sub>Xaa<sub>2</sub>HisXaa<sub>3</sub>]<sub>r</sub>,

wherein Xaa<sub>5</sub> is an amino acid having a free side-chain -NH<sub>2</sub>, m is 0-5 and r is 2-100.

550. (Previously presented) The method of Claim 546 wherein P<sub>2</sub> comprises a sequence which binds Cu(I).

551. (Previously presented) The method of Claim 550 wherein P<sub>2</sub> comprises one of the following sequences:

Mci Xaa<sub>4</sub> Mci,  
Met Xaa<sub>4</sub> Xaa<sub>4</sub> Met,  
Cys Cys,  
Cys Xaa<sub>4</sub> Cys,  
Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,  
Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,  
Gly Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:7],  
Gly Met Thr Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:8],  
Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or  
γ-Glu Cys Gly.

552. (Previously presented) The method of Claim 551 wherein P<sub>2</sub> is Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9].

553. (Previously presented) The method of Claim 531 wherein P<sub>2</sub> comprises a sequence which enhances the ability of the peptide to penetrate cell membranes, reach target tissues, or both.

554. (Previously presented) The method of Claim 553 wherein P<sub>2</sub> is hydrophobic or an arginine oligomer.

555. (Previously presented) The method of Claim 531 wherein at least one of the amino acids of P<sub>1</sub> other than β-alanine, when present, is a D-amino acid.

556. (Currently amended) The method of Claim ~~556~~ 555 wherein Xaa<sub>1</sub> is a D-amino acid[,]  
or His is a D-amino acid, or both Xaa<sub>1</sub> and His are D-amino acids.

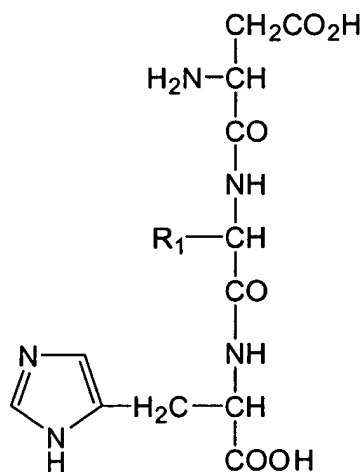
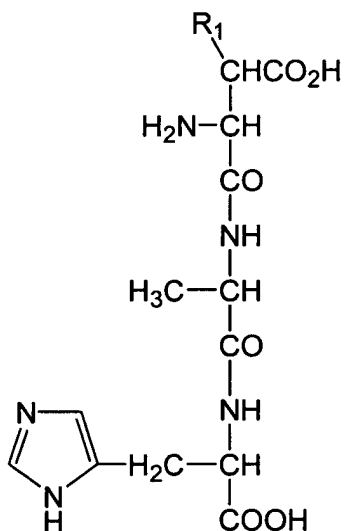
557. (Currently amended) The method of Claim ~~557~~ 555 wherein all of the amino acids of P<sub>1</sub> other than β-alanine, when present, are D-amino acids.

558. (Previously presented) The method of Claim 555 wherein at least 50% of the amino acids of  $P_2$  are D-amino acids.

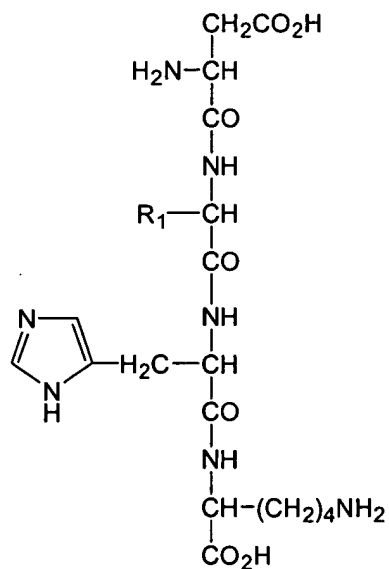
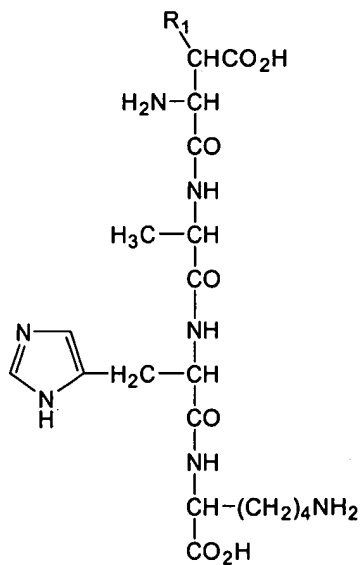
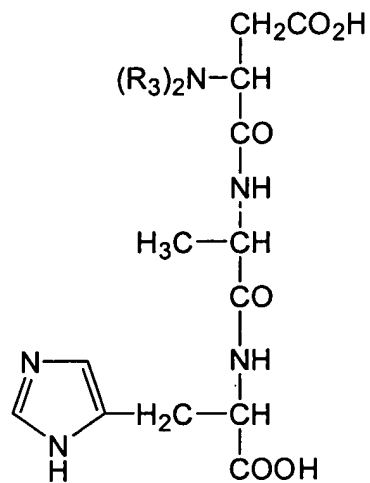
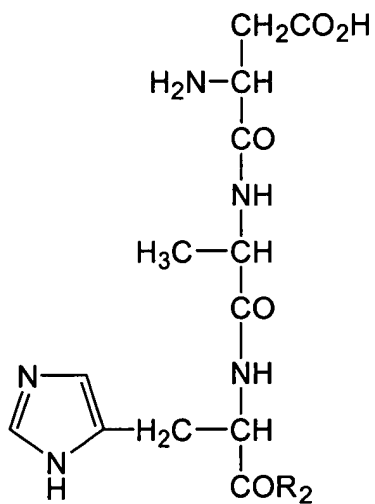
559. (Currently amended) The method of Claim 531 wherein at least one amino acid of  $P_1$ ,] or at least one amino acid of  $P_2$ , or at least one amino acid of  $P_1$  and at least one amino acid of  $P_2$  is substituted with (a) a substituent that increases the lipophilicity of the peptide without altering the ability of  $P_1$  to bind metal ions, (b) a substituent that protects the peptide from proteolytic enzymes without altering the ability of  $P_1$  to bind metal ions, or (c) a substituent which is a non-peptide, metal-binding functional group that improves the ability of the peptide to bind metal ions.

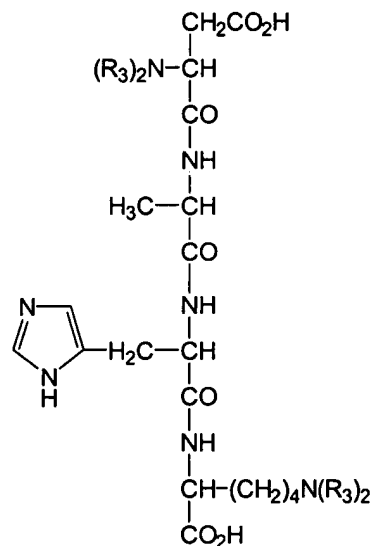
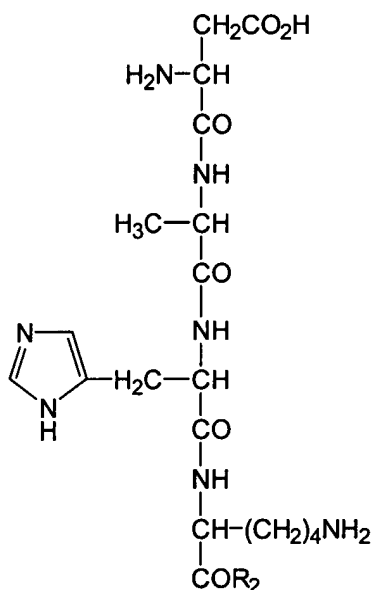
560. (Previously presented) The method of Claim 559 wherein the terminal  $-COOH$  of  $P_1$ - $P_2$  is substituted to produce  $-COR_2$ , wherein  $R_2$  is  $-NH_2$ ,  $-NHR_1$ ,  $-N(R_1)_2$ ,  $-OR_1$ , or  $-R_1$ , wherein  $R_1$  is an alkyl, aryl or heteroaryl.

561. (Previously presented) The method of Claim 559 wherein  $n$  is 0 and  $P_1$  has one of the following formulas:



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wherein:

$\text{R}_1$  is an alkyl, aryl, or heteroaryl;

$\text{R}_2$  is  $-\text{NH}_2$ ,  $-\text{NHR}_1$ ,  $-\text{N}(\text{R}_1)_2$ ,  $-\text{OR}_1$ , or  $-\text{R}_1$ ; and

$\text{R}_3$  is H, a non-peptide, metal-binding functional group or the two  $\text{R}_3$  groups together form a non-peptide, metal-binding functional group.

562. (Previously presented) The method of Claim 561 wherein  $\text{R}_2$  is  $-\text{NH}_2$ .

563. (Previously presented) The method of Claim 531 wherein the method further comprises administering an effective amount of another metal-binding compound in combination with the peptide.

564. (Previously presented) The method of Claim 563 wherein the metal-binding compound binds iron.

565. (Previously presented) The method of Claim 564 wherein the iron-binding compound is deferoxamine mesylate.

566. (Previously presented) The method of Claim 563 wherein the metal-binding compound binds Cu(I).

567. (Previously presented) The method of Claim 566 wherein the Cu(I)-binding compound is a peptide.

568. (Previously presented) The method of Claim 567 wherein the Cu(I)-binding peptide comprises one of the following sequences:

Met Xaa<sub>4</sub> Met,  
Met Xaa<sub>4</sub> Xaa<sub>4</sub> Met,  
Cys Cys  
Cys Xaa<sub>4</sub> Cys,  
Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,  
Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys,  
Gly Met Xaa<sub>4</sub> Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:7],  
Gly Met Thr Cys Xaa<sub>4</sub> Xaa<sub>4</sub> Cys [SEQ ID NO:8],  
Gly Met Thr Cys Ala Asn Cys [SEQ ID NO:9], or  
γ-Glu Cys Gly,

wherein Xaa<sub>4</sub> is any amino acid.

569. (Previously presented) The method of any one of Claims 531-568 wherein the angiogenic disease or condition is a neoplastic disease, a connective tissue disorder, psoriasis, an ocular angiogenic disease, a cardiovascular disease, a cerebral vascular disease, hemophiliac joints, an immune disorder, a benign tumor, hypertrophy, endometriosis, polyposis, or obesity.

570. (Previously presented) The method of Claim 569 wherein the angiogenic disease or condition is a neoplastic disease.

571. (Previously presented) The method of Claim 570 wherein the neoplastic disease is a tumor.



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572. (Previously presented) The method of Claim 571 wherein the tumor is located in the bladder, brain, breast, kidney, liver, pancreas, lung, cervix, ovary, prostate, stomach, intestines, colon, rectum, or uterus.

573. (Previously presented) The method of Claim 570 wherein the neoplastic disease is tumor metastasis.

574. (New) The method of Claim 569 wherein the angiogenic disease or condition is psoriasis.

575. (New) The method of Claim 569 wherein the angiogenic disease or condition is an ocular angiogenic disease.

576. (New) The method of Claim 575 wherein the ocular angiogenic disease is macular degeneration.